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Oncolytics Biotech® and SOLTI Achieve Primary Endpoint in AWARE-1 Study

- Pelareorep and atezolizumab synergize the anti-cancer immune response in HR+/HER2- breast cancer patients

- Pelareorep alone and with checkpoint blockade converts tumors to PD-L1 positive classification

- Oncolytics validates that pelareorep significantly improves immunotherapies

- Company management hosting a KOL event today at 2:00 pm ET

SAN DIEGO and CALGARY, Alberta, April 12, 2021 /CNW/ -- Oncolytics Biotech® Inc. (NASDAQ: ONCY) (TSX: ONC), together with SOLTI, recently announced new clinical data from the AWARE-1 window-of-opportunity breast cancer study showing patients receiving pelareorep plus checkpoint blockade therapy met the trial's primary endpoint. These data are featured in an electronic poster at the American Association for Cancer Research (AACR) Annual Meeting 2021 during Week 1, which is taking place virtually from April 10-15, 2021.

In the poster, data from the twenty HR+/HER2- early-stage breast cancer patients included in AWARE-1's first two cohorts are presented. These patients were treated with pelareorep and letrozole without (cohort 1) or with (cohort 2) the PD-L1 inhibitor atezolizumab (Tecentriq®) prior to surgery. Evaluation of cohorts 1 and 2 is the core objective of AWARE-1, as HR+/HER2- is the breast cancer subtype Oncolytics intends to examine in a future registrational study.

Pelareorep treatment in cohort 1 upregulated tumor PD-L1 expression, induced the generation and expansion of T cell clones, promoted tumor infiltration of CD8+ T cells, and increased the CelTIL score, a measure of tumor cellularity and inflammation associated with favorable clinical outcomes. These desired outcomes were further enhanced in cohort 2 patients, demonstrating pelareorep and atezolizumab synergistically combine to generate an anti-cancer immune response in the tumor and peripheral blood. Notably, cohort 2 met the pre-specified success criteria for the study's primary endpoint (50% of patients with ≥ 30% increase in CelTIL score), with six of ten patients achieving at least a 30% increase in CelTIL score following treatment.

"These exciting AWARE-1 data confirm pelareorep promotes a pro-inflammatory tumor microenvironment, allowing it to synergistically interact with checkpoint inhibitors to train the immune system to fight cancer," said Aleix Prat, M.D., Ph.D., Translational Principal Investigator of AWARE-1, SOLTI President and Head of the Medical Oncology Department at Hospital Clinic in Barcelona. "The data show combining pelareorep with anti-PD-L1

therapy led to increases in CelTIL score and an improvement in the ratio between cytotoxic CD8+ T cells to regulatory T cells. These striking immunological changes are associated with greater therapeutic efficacy and improved clinical outcomes. Collectively, the AWARE-1 results highlight pelareorep's potential to address the unmet need for techniques to enhance checkpoint inhibitor efficacy and strongly support the continued clinical evaluation of pelareorep-checkpoint inhibitor combinations."

Key data and conclusions from the AACR poster include:

- Treatment with pelareorep alone or in combination with atezolizumab increased tumor PD-L1 expression and led to the conversion of PD-L1 negative tumors into PD-L1 positive tumors
- Pelareorep profoundly reverses immunosuppressive tumor microenvironments and promotes immune effector cell infiltration into solid tumors, positioning it as an enabling technology for a variety of immunotherapeutic agents
- Tumor-cell specific pelareorep replication was observed in all evaluated patients following intravenous pelareorep administration
- 60% of cohort 2 patients (n=10) saw a CelTIL increase of at least 30% from baseline (pre-pelareorep administration) to surgery (21-days post-administration), exceeding the study's pre-specified success criteria
- 70% of all cohort 1 and 2 patients (n=20) saw an increase in CelTIL from baseline to surgery
- The addition of atezolizumab enhances pelareorep's ability to generate and expand new anti-viral and anti-tumor T cell clones in the tumor and periphery
- Compared to cohort 1, cohort 2 patients had a higher ratio of CD8+ T cells to regulatory T cells, suggesting pelareorep and checkpoint inhibition enhances inflammation within the tumor microenvironment

Thomas Heineman, M.D., Ph.D., Global Head of Clinical Development and Operations at Oncolytics, commented, "Based on these new results, we have successfully achieved two key objectives of the AWARE-1 study. We've demonstrated synergy between pelareorep and checkpoint blockade therapy, and we've shown pelareorep triggers an adaptive T cell immune response specifically targeting tumors."

Matt Coffey, Ph.D., M.B.A., President and Chief Executive Officer of Oncolytics Biotech Inc. added, "Achieving the primary endpoint in AWARE-1 is a key milestone validating our clinical development strategy. Data indicating that pelareorep and atezolizumab synergistically interact de-risks both our lead breast cancer program and our additional clinical trials evaluating pelareorep-checkpoint inhibitor combination therapies. The data also highlight pelareorep's ability to profoundly reverse immunosuppressive tumor microenvironments and promote immune effector cell infiltration into solid tumors, positioning it as an enabling technology for a variety of immunotherapeutic agents. Moving forward, we expect these data to facilitate the advancement of our lead breast cancer program towards a registrational study while simultaneously bolstering our business development efforts across several indications and immunotherapy treatment regimes."

The electronic poster, titled "*A window-of-opportunity study with atezolizumab and the oncolytic virus pelareorep in early breast cancer (AWARE-1)*" is available for on-demand viewing on the AACR Annual Meeting 2021 e-poster website and on the *Posters & Publications* page of Oncolytics' website (LINK).

Key Opinion Leader Event

Oncolytics will host a Key Opinion Leader (KOL) event today at 2:00 pm ET with Aleix Prat, M.D., Ph.D., Translational Principal Investigator of AWARE-1, SOLTI President and Head of the Medical Oncology Department at Hospital Clinic in Barcelona and Dr. Richard Vile, a Professor of Immunology at the Mayo Clinic, who led the preclinical CAR T study with pelareorep presented earlier this year (link to press release, link to poster). To access the webcast, please click this link.

About AWARE-1

AWARE-1 is an open label window-of-opportunity study in early-stage breast cancer enrolling 38 patients into five cohorts:

- Cohort 1 (n=10), HR+ / HER2- (pelareorep + letrozole)
- Cohort 2 (n=10), HR+ / HER2- (pelareorep + letrozole + atezolizumab)
- Cohort 3 (n=6), TNBC (pelareorep + atezolizumab)
- Cohort 4 (n=6), HR+ / HER2+ (pelareorep + trastuzumab + atezolizumab)
- Cohort 5 (n=6), HR- / HER2+ (pelareorep + trastuzumab + atezolizumab)

The study combines pelareorep, without or with atezolizumab, and the standard of care therapy according to breast cancer subtype. Tumor tissue is collected from patients as part of their initial breast cancer diagnosis, again on day three following initial treatment, and finally at three weeks following treatment, on the day of their mastectomy. Data generated from this study are intended to confirm that pelareorep is acting as a novel immunotherapy, to evaluate potential synergy between pelareorep and checkpoint blockade, and to provide comprehensive biomarker data by breast cancer subtype. The primary endpoint of the study is overall CelTIL score (a measurement of cellularity and tumor-infiltrating lymphocytes). Secondary endpoints for the study include CelTIL by breast cancer subtype, safety, and tumor and blood-based biomarkers.

For more information about the AWARE-1 study, refer to https://clinicaltrials.gov/ct2/show/NCT04102618.

Tecentriq® (atezolizumab) is a registered trademark of Genentech, a member of the Roche Group.

About Breast Cancer

Breast cancer is the most common cancer in women worldwide, with over two million new cases diagnosed in 2018, representing about 25 percent of all cancers in women. It is the second leading cause of death from cancer in women in America, with an estimated 42,000 deaths in the US in 2020.[1]

Breast cancer starts when cells in the breast begin to grow out of control. These cells usually form a tumor that can often be seen on an x-ray or felt as a lump. The malignant tumor (cancer) is getting worse when the cells grow into (invade) surrounding tissues or spread (metastasize) to distant areas of the body.

About Pelareorep

Pelareorep is a non-pathogenic, proprietary isolate of the unmodified reovirus: a first-in-class intravenously delivered immuno-oncolytic virus for the treatment of solid tumors and hematological malignancies. The compound induces selective tumor lysis and promotes an inflamed tumor phenotype through innate and adaptive immune responses to treat a variety of cancers and has been demonstrated to be able to escape neutralizing antibodies found in patients.

About Oncolytics Biotech Inc.

Oncolytics is a biotechnology company developing pelareorep, an intravenously delivered immuno-oncolytic virus. The compound induces selective tumor lysis and promotes an inflamed tumor phenotype -- turning "cold" tumors "hot" -- through innate and adaptive immune responses to treat a variety of cancers.

Pelareorep has demonstrated synergies with immune checkpoint inhibitors and may also be synergistic with other approved immuno-oncology agents. Oncolytics is currently conducting and planning additional studies of pelareorep in combination with checkpoint inhibitors and targeted therapies in solid and hematological malignancies, as it prepares for a phase 3 registration study in metastatic breast cancer. For further information, please visit: www.oncolyticsbiotech.com.

References:

1. "Breast Cancer Statistics and Resources." Breast Cancer Research Foundation. https://www.bcrf.org/breast-cancer-statistics-and-resources

This press release contains forward-looking statements, within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended and forward-looking information under applicable Canadian securities laws (such forward-looking statements and forward-looking information are collectively referred to herein as "forward-looking statements"). Forward-looking statements contained in this press release include statements regarding Oncolytics' belief as to the potential and benefits of pelareorep as a cancer therapeutic; Oncolytics' expectations as to the purpose, design, outcomes and benefits of its current or pending clinical trials involving pelareorep; and other statements related to anticipated developments in Oncolytics' business and technologies. In any forward-looking statement in which Oncolytics expresses an expectation or belief as to future results, such expectations or beliefs are expressed in good faith and are believed to have a reasonable basis, but there can be no assurance that the statement or expectation or belief will be achieved. Such forward-looking statements involve known and unknown risks and uncertainties, which could cause Oncolytics' actual results to differ materially from those in the forward-looking statements. Such risks and uncertainties include, among others, the availability of funds and resources to pursue research and development projects, the efficacy of pelareorep as a cancer treatment, the success and timely completion of clinical studies and trials, Oncolytics' ability to successfully commercialize pelareorep, uncertainties related to the research and development of pharmaceuticals, uncertainties related to the regulatory process and general changes to the economic environment. In particular, we may be impacted by business interruptions resulting from COVID-19 coronavirus, including operating, manufacturing supply chain, clinical trial and project development delays and disruptions, labour shortages, travel and shipping disruption, and shutdowns (including as a result of government regulation and prevention measures). It is unknown whether and how Oncolytics may be

affected if the COVID-19 pandemic persists for an extended period of time. We may incur expenses or delays relating to such events outside of our control, which could have a material adverse impact on our business, operating results and financial condition. Investors should consult Oncolytics' quarterly and annual filings with the Canadian and U.S. securities commissions for additional information on risks and uncertainties relating to the forward-looking statements. Investors are cautioned against placing undue reliance on forward-looking statements. The Company does not undertake any obligation to update these forward-looking statements, except as required by applicable laws.

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